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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/706,759	11/12/2003	Gerald D. Cagle	2442	7815

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EXAMINER	
KIM, JENNIFER M	

ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 03/14/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/706,759	CAGLE ET AL.	
	Examiner	Art Unit	
	Jennifer Kim	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 January 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4-8 and 10* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4-8,10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on January 13, 2006 has been entered.

Action Summary

The rejection of claims 1, 4-8 and 10 under 35 U.S.C. 103(a) as being unpatentable over Lanier et al. (Clinical Therapeutics, July 2002) of record in view of Kim (U.S.Patent No. 5,976,573) and further in view of Ray et al. (Journal of Allergy and Clinical Immunology, 1999) and Castillo et al. (US. Patent No. 6,743,439B1) is withdrawn in view of Applicants' amendment.

Applicants' amendment necessitated new grounds of rejection as follows:

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1, 4-8 and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lanier et al. (Clinical Therapeutics, July 2002) of record in view of Kim (U.S.Patent No. 5,976,573) and further in view of Castillo et al. (US. Patent No. 6,743,439B1) and Hayakawa et al. (U.S.Patent No. 5,641,805, Yanni et al.) of record.

Lanier et al. teach the efficacy of combined fluticasone (nasal) and olopatadine (ophthalmic) in the treatment of allergic rhinoconjunctivitis (allergic rhinitis combined with allergic conjunctivitis). (abstract, conclusion). Lanier et al. teach the effective amount of olopatadine (0.1%) for the treatment of rhinoconjunctivitis. (page 1165 left-hand column third paragraph).

Lanier et al. do not teach the composition comprising olopatadine and fluticasone in a single nasal aqueous composition, specified particle size of fluticasone, pH, viscosity and the amount range of olopatadine (0.4-0.8% (w/v).

Kim teaches aqueous-based pharmaceutical nasal spray comprising fluticasone comprising recommended viscosity of about 50 to 200 cp. (column 5, lines 17-20,

column 4, lines 3-5). Kim teaches the spray comprising the pH fall within the range of about 4.5 to about 7.5. (column 6, lines 58-65). Kim teaches the range of the fluticasone to be utilized in the spray is about 0.001 to about 2 %wt. (column 4, lines 20-27). Kim teaches the particle size of the fluticasone should be no greater than about 50 microns; preferably the particles have an average size of about 1 to about 20 microns. (column 4, lines 15-19). Kim teaches symptoms of allergic rhinitis include nasal itch, congestion, runny nose, sneezing and watery eyes. (column 1, lines 17-25). Kim teaches the aqueous nasal spray affords numerous and important advantages in the treatment of a condition that involves application of a medicament to the surface of the mucosa which line the nasal cavities by delivering a medicament readily to the many portions of the nasal cavities where it can perform its pharmacological function. (column 3, lines 15-25).

Castillo et al. teach a composition comprising olopatadine for ophthalmic use may also be used and administered as topically as a nasal composition. (abstract, column 1, lines 60-65, column 2, lines 10-25, particularly, line 21).

Hayakawa et al. teach topical formulation of olopatadine for the treatment of allergic eye disease with amounts ranging from 0.0001 to 5 % (w/v) and pH within the range of 4.5 to 8. (abstract, column 6, lines 40-49).

It would have been obvious to one of ordinary skill in the art to formulate fluticasone and olopatadine in a single aqueous nasal spray formulation for the treatment of allergic rhinitis because Lanier et al. teach that both combined treatment comprising fluticasone and olopatadine is effective and compatible for the treatment of

allergic conjunctivitis which encompasses allergic rhinitis and because the aqueous nasal sprays afford numerous and important advantages in the treatment of a condition including allergic rhinitis that involves delivering a medicament readily to the portions of the nasal cavities where it can perform its pharmacological function as taught by Kim. Further, the composition comprising olopatadine for ophthalmic use may also be used as topically and can be administrable as a nasal composition as taught by Castillo et al.

One would have been motivated to combine and formulate fluticasone and olopatadine in a single aqueous nasal spray formulation for the treatment of allergic rhinitis in order to achieve direct delivery of a active agents readily to many portion of the nasal cavities and successfully treat the symptoms of allergic rhinitis including nasal itch, congestion, runny nose, sneezing and watery eyes by administer directly to the target nasal tissues in a convenient single formulation. Further, preferred dosage ranges are merely exemplary and serve as useful guideposts for the physician and that it is well known by Hayakawa et al. (Yanni et al.) that safe dosage range of olopatadine lies between 0.0001 to 5 % w/v. One of ordinary skill in the art would optimize the dosage considering the severity of the allergic rhinoconjunctivitis patients disclosed by Lanier by increasing dosages of olopatadine within the safe range taught by Hayakawa et al. in order to successfully treat severe allergic rhinitis patients disclosed by Lanier.

For these reasons the claimed subject matter is deemed to fail to patentably distinguish over the state of the art as represented by the cited references. The claims are therefore properly rejected under 35 U.S.C. 103.

None of the claims are allowed.

Response to Arguments

Applicants' arguments filed January 13, 2006 have been fully considered but they are not persuasive. Applicants argue Lanier et al. do not disclose or suggest incorporating olopatadine into an intranasal composition and does not disclosed or suggest incorporating olopatadine into an intranasal product for alleviating nasal symptoms. This is not persuasive because the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, Lanier et al. teach the efficacy of combined regimen of fluticasone and olopatadine is useful for the allergic rhinoconjunctivitis and that Castillo et al. teach that a composition comprising olopatadine can be employ topically as a nasal composition. Therefore, it would have been obvious to one of ordinary skill in the art to formulate the combined regimen taught by Lanier in a convenient single nasal formulation in order to achieve advantage of delivering two active agents in a single convenient formulation. One of ordinary skill in the art would have been motivate to formulate the combined regimen taught by Lanier in a nasal formulation because both active agents are individually well known by cited art to be formulated in nasal

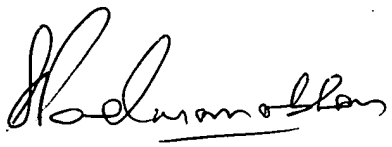
composition. Applicants argue that Applicants' claims recite a method of treating allergic rhinitis comprising intranasally administering a composition comprising at least 0.4%(w/v) olopatadine and a specified amount of a steroid selected from the list recited in Applicants' claim 1. This is not persuasive because as anyone of ordinary skill in the art will appreciate, preferred dosages are merely exemplary and serve as useful guideposts for the physician. There are, however, many reasons for varying dosages, including by orders of magnitude; for instance, an extremely heavy patient or one having an unusually severe allergic rhinitis patients would require a correspondingly higher dosage. Furthermore, it is routine during animal and clinical studies to dramatically vary dosage to obtain data on parameters such as toxicity. For these and other self-evident reasons, it would have been obvious to have used much higher dosages of olopatadine in order to successfully treat allergic rhinitis patients disclosed by Lanier. Applicants argue that Castillo et al. simply teaches that the vehicle is suitable for nasal administration and not that any particular olopatadine compositions are suitable for nasal administration. This is not persuasive because Castillo et al. clearly teach that olopatadine composition is well known to be administered nasally and it is noted that Applicant's broad claim 1 and 16 drawn to "comprising" does not exclude the vehicles employed by Castillo et al. that are suitable for nasal administration. Applicants next argues that the selection of olopatadine as an anti-allergy agent to be combined with a steroid in an intranasal composition provides a special safety feature that conventional anti-histamine agents do not and the article Brockman et al., demonstrates the different effects or consequences that olopatadine and antihistamine

agents have on interaction with cell membranes and unlike conventional antihistamine agents, olopatadine is unlikely to cause histamine release or non-specific cell membrane damage. This is not persuasive because Brockman et al. do not show the specific combination of instant invention (olopatadine and fluticasone) and that Lanier et al. already demonstrated the advantage of olopatadine with fluticasone compared with a conventional antihistamine with fluticasone. It is well known by Lanier et al. that the combination of olopatadine and fluticasone is more effective than concomitant use of fluticasone plus conventional antihistamine (fexofenadine) for overall treatment of the signs and symptoms of induced allergic rhinoconjunctivitis. That applicant may have determined a mechanism by olopatadine not causing non-specific interaction with cell membranes that can lead to cell damage gives the better pharmacological effect compared to conventional antihistamine (fexofenadine) does not alter the fact that Olopatadine combined regimen with fluticasone has been previously used by Lanier to obtain the same pharmacological effects of treating rhinoconjunctivitis. Thus, the claims fail to patentably distinguish over the state of the art as represented by the cited references.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer Kim whose telephone number is 571-272-0628. The examiner can normally be reached on Monday through Friday 6:30 am to 3 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Sreenivasan Padmanabhan
Supervisory Examiner
Art Unit 1617

Jmk
March 3, 2006